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Robert L. Stephenson III, M.P.H.
Director, Division of Workplace Programs, CSAP
5600 Fishers Lane
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Dear Mr. Stephenson,

This letter will convey to you my comments regarding the 'Notice of Proposed Revisions' to the Mandatory Guidelines for Federal Workplace Drug Testing Programs, as published in the Federal Register, Volume 66, Number 162, August 21, 2001.

Changes to the Definition of 'Substitution':

The Secretary is proposing a change to the definition of a 'Substituted Specimen' by changing the creatinine from ≤ 5 mg/dl to < 5 mg/dl. However, I do not believe that this goes far enough. As cited on page 43877, the DOT's Office of Drug and Alcohol Policy and Compliance has conducted a study focusing on paired measurements of creatinine and specific gravity.

In that study, two subject specimens had specific gravity determinations of 1.001 and creatinine concentrations that can be statistically defined as substituted. The measured creatinine concentration for these two specimens were 5.1 and 5.2 respectively, while both had specific gravity determinations of 1.001. Our typical coefficient of variation (CV) is between 2.5% and 5.0% for creatinine controls targeted at 3.8 mg/dl and 7.1 mg/dl. These CVs are much more stringent that the range of ± 20% of the mean that is considered acceptable in NLCP proficiency testing. Acceptable ranges for each of these reported creatinine results are listed in the following table.

Creatinine (mg/dl)	Acceptance range: 2.5 % CV	Acceptance range: 5.0 % CV	Acceptance range: ± 20%
5.1	4.85 – 5.36	4.59 – 5.61	4.08 – 6.12
5.2	4.94 – 5.46	4.68 – 5.72	4.16 – 6.24

In all cases, repeated creatinine analyses have the potential to be reported as substituted for these two donor samples known to be real human specimens. It would be interesting to know what the CVs for creatinine controls were at Kroll Laboratory at the time this study was conducted. I would expect to obtain similar findings by applying their CV.

Additionally, I have gathered some creatinine concentration distribution data from our laboratory for both regulated and non-regulated specimens that meet the current definition for substitution. I also have the same data from another certified laboratory for their regulated specimens. This data is summarized in the table below.

Conc. (mg/dl)	ATN-DOT	ATN-NDOT	SBMF-DOT	Total
0.0 – 0.4	112	147	74	333
0.5 – 0.9	12	31	2	45
1.0 – 1.4	8	22	1	31
1.5 – 1.9	5	17	3	25
2.0 – 2.4	10	9	3	22
2.5 – 2.9	10	9	2	21
3.0 – 3.4	17	14	1	32
3.5 – 3.9	9	17	6	32
4.0 – 4.4	10	16	1	27
4.5 – 4.9	15	48	5	68
5.0	2	9	2	11

As you can see, these data demonstrate a bimodal distribution of creatinine concentrations with one mode at < 0.5 mg/dl and a second at > 4.5 mg/dl. No one would dispute that specimens with creatinine concentrations approaching zero should be considered as substituted. The issue is those specimens about the 4.5 mg/dl mode. As shown in an earlier paragraph, from a statistical standpoint, these specimens might easily have been reported as dilute, not substituted. A 4.5 mg/dl combined with a 7% CV can acceptably yield a result of 5.1 mg/dl. Conversely, a 5.7 mg/dl with a 7% CV can yield a substituted result of 4.9 mg/dl. I would pose for the Secretary's consideration the thought that specimens about the 4.5 – 5.0 mg/dl mode include specimens that cannot, with statistical certainty, be defined as substituted.

At the SOFT convention in New Orleans earlier this month, Dr. Barry Sample of Quest Diagnostics presented some statistical data in graphical format. This data also demonstrated a bimodal distribution for creatinine concentrations with modes at <1 mg/dl and ≃ 5 mg/dl. With the NLCP requirement that certified laboratories submit a Non-Negative Specimen Listing (NNSL) that includes creatinine and specific gravity results for all specimens reported as 'Substituted', it should be a relatively easy task to determine if this bimodal distribution holds true amongst all certified laboratories.

Another point to consider is the fact that creatinine is an endogenous substance. The analysis of this analyte should not be treated in the same manner as benzoylecgonine or THCA. The drugs mentioned should not be present in a donor specimen, as they are exogenous compounds. Establishing a concentration above which the specimen is defined to be positive and below which it is negative is understandable, as the definitions are purely arbitrary. We all realize that a specimen containing exactly 15.0 ng/ml of THCA has a fifty percent chance of being reported as negative. If a retest of a specimen reported to contain 15 ng/ml of THCA is requested, any concentration of THCA at or above the second laboratory's LOD is still considered positive.

However, creatinine must be present to be considered a valid specimen. Again, the definitions of 'substituted' and 'dilute' are arbitrary definitions. And as it is with the THCA analogy, a creatinine of 5.0 mg/dl (or 4.9 mg/dl with the proposed definition) and SG of 1.001, may be reported as 'substituted' fifty percent of the time and as 'dilute' the other fifty percent of the time. When a retest is requested however, it is just as likely that the original results will be overturned as it is that they will be reconfirmed. In cases where the retest overturns the original result, the donor incurs the expense of the retest and the original testing laboratory is made to look incompetent, when in fact, neither laboratory is in error.

I would suggest that the Secretary redefine 'substituted' as < 2.0 mg/dl with a SG of < 1.002. Concurrent with this change, include in the definition of 'invalid' specimens those with creatinine concentrations of 2.0 – 5.9 mg/dl (or 4.9) and SG determinations of < 1.002. Precedence for this is

found in the proposed guidelines with respect to pH. The proposed rules define as 'invalid' specimens with pH in the ranges of 3.0 – 3.9 and 10.0 – 10.9, essentially adding a 'buffer' between adulterated and normal specimens. By mimicking this 'buffer' in the definition of substitution, specimens that physiologically improbable will be reported as substituted, while those in that statistically gray area are considered invalid.

Specimen Validity testing – Oxidants:

If nitrite testing is to be made mandatory, I propose that an 'invalid' range be defined for this analyte as well. This would mimic the pH changes and my proposed creatinine/SG definitions. Once again, nitrite is an endogenous substance and an 'invalid' range of 200 –499 ug/ml will provide for a 'buffer' between specimens containing normal concentrations of nitrites and adulterated specimens.

With respect to section 2.4(g)(v), I am unclear what a certified laboratory must perform that qualifies as 'additional testing'. In conversations with RTI staff, ATN was told that the laboratory may perform an initial oxidizing adulterant test. When positive, this initial test may be followed by a re-analysis for oxidants on a second aliquot. If both the initial and second aliquot tests are positive, the laboratory may report the specimen as invalid without any further testing. At the recent SOFT meeting, the RTI staff distributed an SVT spreadsheet listing initial and confirmatory validity testing methods. This same information was listed as an acceptable procedure resulting in a final result of 'Invalid: Abnormal Oxidant Activity.' This seems to be in direct conflict with a statement in the background information to the proposed rules on page 43878. If this is not the intent of section 2.4(g)(v), I would urge the Secretary to permit this testing procedure.

For the number of specimens reported as adulterated, it seems unnecessary that all laboratories have the capability to identify and quantitate specific oxidizing adulterants. Several laboratories currently perform testing for specific adulterants. It seems reasonable to allow the original laboratory to report specimens as 'invalid' because of excess oxidant activity. Allow the employer and/or MRO to decide whether circumstances (reason for test) warrant the expense of performing specific adulterant testing at a second certified laboratory. For example, if the test is a pre-employment collection, direct an observed re-collection, while in all other cases, initiate specific adulterant testing at a certified laboratory with the specialization to conduct such testing.

Along these lines, here is something else to consider. Most certified laboratories do not have the expertise in house to perform ion chromatography, capillary electrophoresis or a number of other testing methods required to identify and confirm the presence of specific adulterants. An alternate testing option would be for the NLCP to enter into a contractual agreement with a laboratory that can specialize in adulteration testing. Laboratories would then forward specimens for adulteration confirmation.

Section 2.4(g)(v)(A) directs the laboratory to conduct additional validity tests because of abnormal color, odor or excessive foaming. Please define an abnormal color or odor. Is a green or red specimen abnormal? If so, how green or red? Should the laboratory test each processing employee for color-blindness? Does this section require that the laboratory smell every specimen? If so, what is an abnormal odor and how do we train employees to recognize these abnormal odors? In the SVT spreadsheet distributed by RTI at the SOFT meeting, testing methods for halogens included odor as the initial test followed by a colorimetric test as the confirmation. Similarly, surfactant testing methods list a 'foam/shake' initial test followed by a colorimetric assay. I realize that in both these situations, the specimen is to be reported as invalid, but someone will eventually challenge these results in a labor dispute. How is the laboratory to defend the findings of an abnormal odor? It was also noted that only one certified laboratory was currently performing anionic surfactant testing. Is it required that all certified labs validate and maintain anionic surfactant testing methods? I recommend that Section 2.4(g)(v)(A) and related (sections 2.4(g)(5)(i) and 2.5(j)(3) be deleted from the final rule. This section is ambiguous and laboratories are not prepared to conduct color, odor or anionic surfactant testing.